A REVIEW ON SEMISOLID TOPICAL PREPARATION

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Abstract

Already in ancient times, semisolid preparations for cutaneous application, popularly known as ointments, played an important role in human society. An advanced scientific investigation of "ointments" as dosage forms was set off in the late fifties of the previous century. It was only from then on that the intensive physico-chemical characterization of ointments as well as the inclusion of dermatological aspects led to a comprehensive understanding of the various interactions between the vehicle, the active ingredient, and the skin. In the meantime, many researchers have been involved in optimizing semisolid formulations with respect to continuously changing therapeutic and patient needs. Aspects that have been dealt with are the optimization of dermato-biopharmaceutical properties and many different issues related to patient's compliance, such as skin tolerance, applicability, and cosmetic appeal. Moreover, processing technology has been improved and analytical techniques developed and refined in order to enable improved characterization of the formulation itself as well as its interaction with the skin.

Keywords: - *semi-solid dosage form, dermatology products*

1. INTRODUCTION

Skin is the most important and has a complex structure. It is the largest and easily accessible organ of living animals, however here the discussion is limited to human beings.[1,2] It is estimated that an average adult human has a skin surface area of 1.8 to 2.0 m^2. Morphologically skin forms the most complex structure comprising of multiple layers with thickness ranging from 0.5 to 4 mm.[3,4] Hence, understanding the skin morphology becomes essential before discussing skin diseases, route of administration and permeation/ penetration of chemicals (active or inactive) through skin.[5,6]

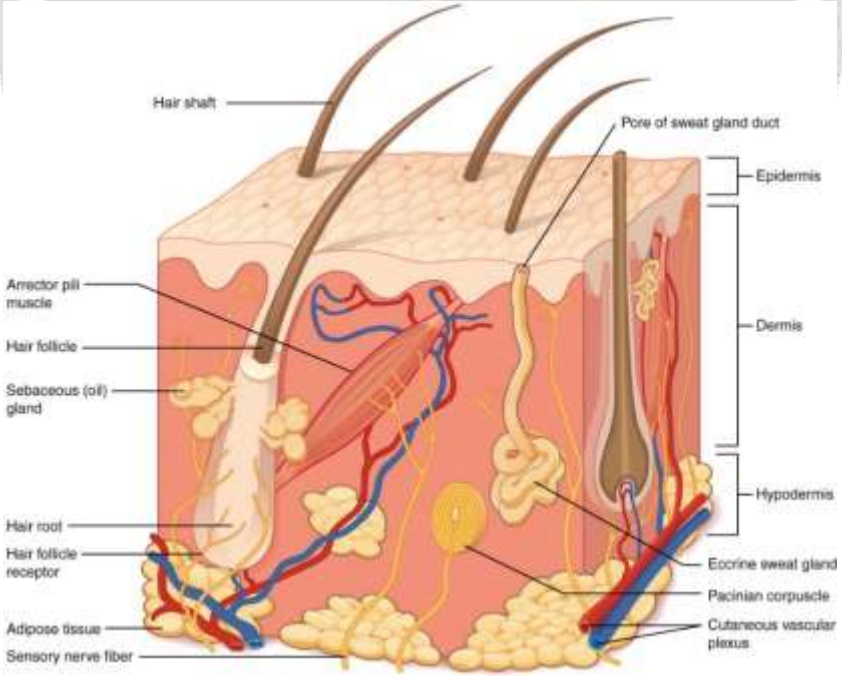


Figure 1. Diagrammatic representation of layers of Skin.

Skin has three layers majorly viz. epidermis, dermis and hypodermis.[7] Stratum corneum forms the outer most layer of epidermis which forms the major barrier (rate limiting layer) for most of the actives as well as foreign particulate matter including microorganism to enter through skin.[8,9] Dermis and hypodermis have numerous blood vessels and consists of hair follicles, sweat glands and other structures like sebaceous glands.[10]

Topical dosage forms are solutions, suspensions, creams, gels, ointments or pastes containing one or more active ingredients dissolved or uniformly dispersed in a suitable base.[11,12] Depending on the disease condition and desired therapeutic effect the dosage form design is selected.[13] The excipient selection depends largely on dosage form being developed, which forms the most critical part of development in Topical dosage form as it will decide the characteristics of end-product which is directly impacting active ingredient efficacy and product elegance.[14,15]

With increase in understanding on skin morphology and route of penetration, interest on skin formulation (Topical Semisolid Dosage form) has tremendously increased in pharmaceutical Research over the last few decades.[16,17] Conventional emulsions, creams ointments and lotions are still acceptable and cost-effective option available for skin disorders.[18]

Indian Pharmaceutical product manufacturers contribute around 30% to 35% of generic market globally due to potential research scope and low conversion cost. Various pharmaceutical sectors are effortlessly developing, approving and manufacturing Generic Drug Products for global supply.[19,20,21] Generic Drug Products are bioequivalent cost-effective replacement for Branded / Patented formulations which could be used as alternative with equivalent therapeutic effectiveness. While discussing development of generic Topical Semisolid dosage form; selection of excipients, its quantity, grade, selection of right vendor as well as manufacturing process used to produce Topical Products are considered as critical attributes for success rate of formulation.[22,23,24] Topical products are considered to be complex products where the therapeutic effect depends on drug transport from product to skin surface and from skin surface to site of action, hence the micro-arrangement of excipients and actives within the formulation.[25,26,27]

Semisolids are the product for the use on skin and mucous membranes. It may used for the treatment of pathological conditions and may also protect the body from harmful conditions. These semisolid preparations are used to protect over the time and produces the therapeutic effect through the occlusions.[28,29,30] These may contain the plastic rheological behaviour. These behaviours may allow the semisolid to retain the shape and size of the film and act by the outside force. For localized drug delivery these semi solid preparations are use.[31,32] In recent era, these semisolid preparations are used for the systemic delivery of various types of drugs. These give the significance in pharmaceutical dosage forms. It may be applied on the skin, cornea, rectal tissue, nasal mucosa, vagina and external ear lining.[33,34,35]

These preparations may contain two phases. One is external phase and another one is internal phases. These active ingredients are present in both the phases.[36,37] Three-dimensional structure may characterize the semisolids preparation.[38]

Ideal Properties of Semisolid Dosage Forms

1. Physical Properties

- Smooth texture
- Elegant in appearance
- Non dehydrating
- Non gritty, greasy and non-staining

2. Physiological Properties

- Non irritating
- Do not alter membrane / skin functioning
- Miscible with skin secretion
- low sensitization index

3. Application Properties

- Easily applicable with efficient drug release
- High aqueous washability

4. Storage Properties

- Storage of semisolids at 25°C.
- It should not allow to freeze and stored in a well-closed container.[39,40,41,42]

2. FACTORS AFFECTING SKIN PENETRATION

➢ gastro intestinal absorption and skin penetration both are same by the rate of diffusion, pH, physicochemical property, vehicle used and concentration.

➢ In physicochemical factor the skin penetration is hydration state of stratum corneum. It may affect the rate of penetration of skin.[43,44,45]

➢ to the absorption site, solubility of a drug determines the concentration. The rate of transport influences the partition coefficient.

➢ In absorption rate and the molecular weight an inverse relationship is appeared.

➢ large molecule penetrates slow then small molecules. There is a co relation between the size and penetration rate due to molecular size.[46,47,48]

3. TOPICAL DRUG DELIVERY

An Intestinal lipid pathway and proteinaceous cellular component is present in between the layer of skin and stratum corneum.[49,50] By the help of tortuous and intercellular path drug molecules are penetrated into the skin. By the help of solvents and enhancers are used for the transport of topical drugs.[51,52] It may also transport by the drug by the hair follicles, transcellular and sweat ducts. The molecules which are presents are only penetrate through the skin.[53,54] Ointment may retain the significance of trans epidermal of water and drug transport by the hydrated skin. dermatitis, psoriasis, and warts are the barrier of skins.[56,57] These are the geared of drugs towards skin diseases. Driving forces are generated between the formulation and site of action it may help the drug to penetrated into the skin.[58,59] A thermodynamically activity may generate large driving forces. It helps to transport the formulation through the skin at a small amount of fraction.[60,61] In super-saturated conditions the thermodynamically activity has a greater unity and may enhanced the drugs through skin. It is in metastable state and it may convert back into their original sizes with changing in the flux of drug.[62,63,64]

4. MATERIALS USED FOR MEDICINAL PREPARATION

Physiochemical properties like solubility, molecular weight, pH and stability are shown for the composition of medicinal preparation.[65,66] The ingredients which are required for the manufacturing of medicinal preparation are been given by according to pharmaceutical law, patent law. Packaging and stability are also considered. Solvents are also used in this.[67,68] Vehicles like preservatives, antioxidants, dyes, and buffers are also used for this preparation. No means trivial may have the composition of suitable, well-balanced, and stable preparation.[69,70,71]

5. QUALITY REQUIRED FOR MEDICINAL PREPARATION

Medicinal preparation is required a quality criteria. Quality is the main factor for this preparation.[72,73] This are also help for the development of medicinal products. Every cosmetic and medical device required validated and manufactured according to high quality standards. All ingredients should be characterized by high purity and quality.[74,75,76] These manufactures required certification and quality assurance processes. Each final batch should undergo testing like chemical, physical and microbiological stability. Stress test are performed for the determination of in-use and storage stability. AMG is also applied for every formulation.[77,78,79]

6. PHARMACOKINETIC OF TROPICAL AGENTS

Tropical agent's pharmacokinetics were determined by physiochemical characteristics of active ingredients. It may also depend on vehicles characteristics and the skin condition.[80,81] Different pharmaceutical concepts have different vehicles system and these may affect the pharmacokinetics of medicinal preparation. Skin conditions are also paly a most important role. The preparation selection is based on pharmacokinetic criteria.[82,84,85]

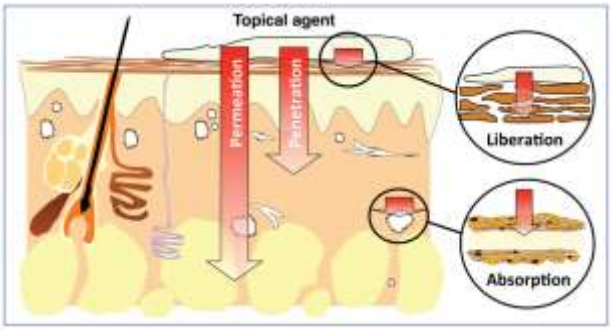


Figure 2. Pharmacokinetics of topical agents

Pharmacokinetic principle may have three overlapping functioning process. The epicutaneous of tropical agents may dissolved and suspended the ingredient released.[83,84] Only this preparation may become the skin bioavailability. Vehicle composition may liberate the rate of physiochemical properties as well as properties of skin.[85,86] The skin may be inter and intra which may be changes the healing process. The therapeutics effects may also varies. The stratum corneum has play an important role as boundary layer and a drug uptake.[87,88] This stratum corneum has reservoir function. Semi solid preparations may transfer the stratum corneum within a few minutes before residue removed from the skin.[89,90] Active ingredients contain numerous microcompartments at the skin layers. Some factors may impact this process. diffusion distance, diffusion surface and concentration differences are the most important in this process.[91,92] Hagen-Poiseuille's law of hydrodynamic pressure gradient show the thermodynamic activity and convection processes.[93,94] The active ingredient may pass through the skin layer and may diffused into deeper tissue layers. These may be eliminated by absorption through the microvascular system or by enzymatic degradation by sessile cell.[95,96,97] For diffusion process various routes is available. Intercellular route is the most important passage marked as hydrophilic and a lipophilic route. This utilizes the hydrophilic of ceramides and water molecule interacting for diffusion.[98,99,100] For matrix penetration, ceramides have flexible lipophilic side chains. dermatological indication and pharmacodynamic properties of an active ingredient may used for the optimization of concentration-time profile.[101,102] Indication based approach is optimized the therapeutic efficacy. The diseased skin contains chemical and physical factors.[103]

7. COMBINATION PREPARATION AND PLANNING OF TREATMENT

For clinical treatment, some combination of active pharmaceutical ingredient. Physicochemical properties in active ingredient may be optimized.[104] Combination preparation were pharmaceutical represented. pharmaceutical ingredients of two ingredient may combined and have clinical efficacy to improve the patient treatment.[105,106] antifungal agent and corticosteroid combination may have inflammatory cutaneous mycoses. combination therapy has extemporaneous formulations in medicinal products.[107,108] Pharmaceutical incompatibilities and interactions are not trivial. On skin lesion the polyvalent preparation were applied without clearing the surface.[109,110] Other therapeutic has antibiotic/antiseptic agents, corticosteroids and local anaesthetic agents has not complete the requirement of the treatment.[111,112] through specific and nonspecific adverse effects pose and inefficient risk is undue. Mono preparation of sequential are used in the combination of therapeutic. 30minute interval is shown it reduces the risk of interaction in between the ointment and the skin.[113,114]

For optimization of therapeutic intervention are able to order by medical, economic and aspect of practical.[115] These are used in severe and chronic disease. Disease acuteness, induction and maintenance of therapy may prove the successfulness. Pathogenesis of disease may have therapeutic components.[116,117] These processes may contain physical, cosmetic, pharmacological and physiotherapeutic. For tropical applications in medicinal products suitable vehicles are used and the dosage form may produce the important role.[118,119] Only one concentration is used into the active ingredient. These medicaments are having some chances in curative treatment.[120,121]

8. ADVANCED MEDICAL DEVICES USED IN THE TREATMENT OF SKIN DISEASES

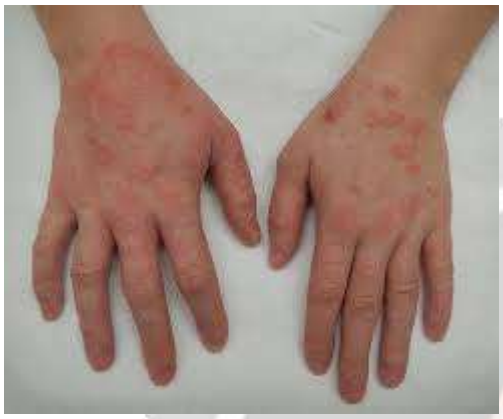
There are three possibilities by which semi solid preparation may applied on the skin. These are tropical drugs, cosmetics and medical devices.[122,123] Drugs may be defined as a substances or mixer of substances which are used for the treatment or administration to heal and prevent diseases.[124,125] It may also used for the correction of pharmacological, immunological and metabolic means.[126]

Medical devices are the substances which are used for the prevention, monitoring, treatment and alleviation of host from the body.[127] It is not done by pharmacological or immunological means or by metabolic means.

Medical devices are different form any other process by the legal basis. A compressive licence is required for the drug supply to the markets.[128,129]

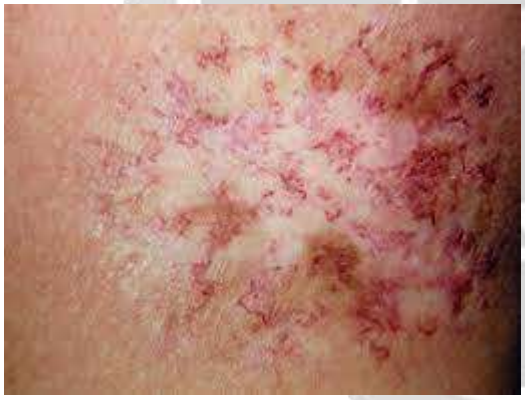
Atopic dermatitis

It is a skin inflammatory chronic disease. It may affect the children. It may characterise by xerosis, erythematous and pruritus lesions with trans epidermal. Some microorganism is also used in this skin infections.[130,131] one semi solid preparation is used for the management of atopic dermatitis. For the reduction of signs and symptoms of atopic dermatitis nonsteroidal multicomponent are used. corticosteroid and calcineurin are used in multicomponent treatment for distinguished from other topical preparations. Atopic dermatitis is the treatment which may treat mild to moderate diseases in child and adult.[132,133]



X-ray- or radiation-induced dermatitis

In cancer therapy, radiotherapy is most important treatment. Dose depended skin reaction may receive radiation induced dermatitis.[134] These may be ringing from mild erythema to moist desquamation. double blind and vehicle controlled the efficacy and tolerability of medical devices.[135,136]

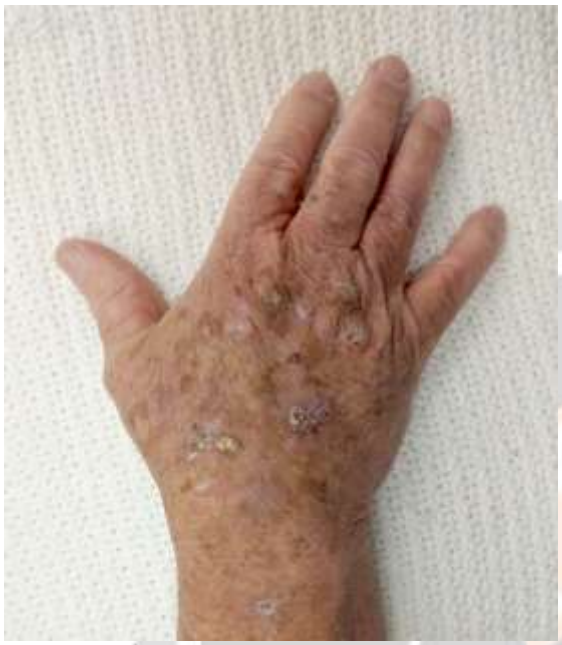


Seborrheic dermatitis

This skin disease manifests the scalp and the face and is associated with scaling.[137] Antifungal agents and calcineurin inhibitors are the medical device and may reduce the seborrheic dermatitis.[138]

Actinic keratosis

It may be defined as a scaly, erythematous lesions produce by exposure of sun for many years. It was only found by sun terraces on the skin. It was the neoplasias in the fair skinned population and may produces nonmelanoma skin cancer.[139,140] In situ it was consider as a squamous cell carcinoma. It may transform into squamous cell carcinoma. These may require early treatment. It may be characterized by hyperkeratotic, scaling, lesions by sun exposed skin sites. UV radiation may produce the nonmelanoma skin cancer.[141,142] This preparation is already established for the prevention of epithelial cutaneous lesions. Curettage, cryotherapy, excision and laser therapy is used for the treatment and prevention of squamous cell carcinomas.[143,144] These lesions have greater importance. Liposomal sunscreen is used as a medical device in that.[145,146]



Hypertrophic scars and keloids

For the treatment of scars corticosteroids and silicones are used. Silicone gels are easy to handle.[147] The mechanism of action of silicone has hydration of stratum corneum by which the trans epidermal water loss is reduced.[148] Cytokine signal transformation from keratinocytes to dermal fibroblasts. It may inhibit the proliferation of fibroblast and should reduce the collagen synthesis.[149,150] Self-driving silicon gels are used for the prevention and treatment of hypertrophic scars and keloids in medical devices. Silicon gels has lower height.[151]

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